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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,586	05/03/2002	Dan L. Eaton	10466/353	2703

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KNOBBE, MARTENS, OLSON & BEAR, LLP
2040 MAIN STREET
IRVINE, CA 92614

EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/063,586	Applicant(s) EATON ET AL.	
	Examiner Claire M. Kaufman	Art Unit 1646	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 14 February 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-8 and 11-13*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Advisory Action Continued:

The majority of Applicants' arguments appearing in the Remarks filed on 2/14/05 were addressed in the previous Office action and remain unpersuasive. All rejections are maintained for reasons of record. New arguments only are addressed here.

Under utility, Applicants argue (p. 7-9) that the present situation is like that in *Cross* or *Fujikawa* in which *in vitro* testing supported use *in vivo,* and supports reliance on a "reasonable correlation" between expression data and diagnostic utility. The argument has been fully considered, but is not persuasive. At issue is **not** whether *in vitro* microarray/expression data can *per se* support use of differential expression for diagnostic purposes. The issue in this application is the insufficiency of disclosure to support a specific and substantial or well established utility or to allow the skilled artisan to use the claimed invention without undue experimentation. Because as previously discussed there is critical information lacking which includes: whether differences in nucleic acid expression of PRO1357 were significant, under what conditions differences could be detected, and what levels (relative or absolute) were detected in tumor and normal control, the skilled artisan cannot use (whether *in vivo* or *in vitro*) the claimed invention. It is possible that with the lacking information in hand, the skilled artisan could make a reasonable correlation between at least nucleic acid expression data and diagnostic utility. Such a correlation may not be extendable to binds the encoded polypeptide or binding antibody and diagnostic utility.

Applicants argue (p. 13) that in addition to references previously submitted, those of the Alberts et al. and Lewin textbooks and Zhigang et al. support the correlation between cDNA/mRNA expression and protein expression. The argument has been fully considered, but is not persuasive. The argument of correlation between nucleic acid and protein expression has been previously addressed, but it should be noted that with the Office maintaining that the instant specification does not support utility for the polynucleotide as a diagnostic tool, a diagnostic use for the protein or antibody is likewise not supported, regardless of whether their levels correspond.

Under enablement, Applicants argue (p. 19-20) that a use of the encoded PRO1357 polypeptide is creation of diagnostic and therapeutic antibodies. The argument has been fully considered, but is not persuasive. If the polypeptide is not enabled, then an antibody which binds it is also not enabled.

Under written description, Applicants argue (pages 20-21) that the training material supports written description for hybridizing nucleic acids and non-identical polypeptides, for example, and that patents have been issued which claim variants. The argument has been fully considered, but is not persuasive. Unlike in the training material, at issue is a polypeptide which is itself or which must be encoded by a nucleic acid which is naturally occurring because it exists in normal and tumor cells. Yet neither the claimed polypeptide nor the encoding nucleic acid need not be identical to the only disclosed naturally occurring polypeptide or nucleic acid, respectively, meeting the functional limitation in the claims. This is not a case in which a polypeptide must be able to bind protein X, for example. In that situation, the polypeptide need not be naturally occurring. The instant claims exclude all but a small subset of structural variants, being limited by the required function to particular naturally occurring variants. Also, the ability to find polypeptides and encoding nucleic acids which do meet all the claim limitations using "routine methodology" such as Western or Northern Blotting or PCR does not provide written description because the inventors were not in possession of those other nucleic acids and could not have readily envisioned them. Further, each application is examined on its own merits.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (571) 272-0829.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (571) 273-8300. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office. **Please** advise the examiner at the telephone number above before facsimile transmission.

Claire M. Kaufman, Ph.D.
Patent Examiner, Art Unit 1646
March 7, 2005

LORRAINE SPECTOR
PRIMARY EXAMINER